a monoclonal human [sequence] immunoglobulin comprising a VkL19 segment, a Jk2 segment, and a light chain CDR3 region comprising the sequence QQANSFPYT (SEQ ID NO:69), and

a monoclonal human [sequence] immunoglobulin comprising a VkL15 segment, a Jk2 segment, and a light chain CDR3 region comprising the sequence QQYDSYPYT (SEQ ID NO:70).

REMARKS

STATUS

Claims 10, 12, 13, 14, 18-29, and 31-53 are under examination. Claims 10, 12, 18-21, 31-36, 38, 39, 41-49 and 52 were canceled. Claims 13, 22-29, 37, 40, 50-51 and 53 were amended. After entrance of the amendment, claims 13, 14, 22-29, 37, 40, 50-51 and 53 are pending.

Claims 13 and 14 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not described in the specification. Claims 13, 14, 22-29, 37, 40, 50 and 51 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. Claim 35 and 38 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not described in the specification under 37 C.F.R. § 1.801-1.809. Claim 38 is objected to under 37 C.F.R. § 1.75(c), as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 13, 14, 35 and 38 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Claims 10, 12, 18-21, 31-34, 38-39, 41-49 stand rejected under 35 U.S.C. § 103(a) as obvious over Cobbold *et al.* (U.S. Patent No. 5,690,933) and Queen *et al.* (U.S. Patent No. 5,530,101).

Support for the amendments to claims 13, 22-29, 37, 40, 50-51 and 53 is found throughout the specification and in the claims originally filed. Claim amendments are for purposes of improved clarity or consistency of claim language unless otherwise noted. No claim amendment should be construed as an acquiescence in any ground of rejection.

The claims were amended as suggested by the examiner and to expedite prosecution. Specifically, the examiner invited Applicants to claim CD4-specific human monoclonal antibodies with all of the appropriate sequences that provide for binding CD4.

Applicants use the paragraph numbering in the Office Action in responding to the examiner's remarks.

Rejections Under 35 U.S.C. § 112, first paragraph

6. Claims 13 and 14 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not described in the specification. Specifically the examiner stated that the specification as originally filed does not provide support for the invention as now claimed: "similar affinity" and "at least about" language. In order to expedite prosecution, Applicants have amended claim 13 in a manner that renders this rejection moot. Applicants believe that claim 13 is now in condition for allowance.

Therefore, the rejection of claim 13 under 35 U.S.C. § 112, first paragraph, should be withdrawn. Insofar as claims 14, 50 and 51 depend on claim 13, Applicants request that the corresponding rejection of claims 14, 50 and 51 under 35 U.S.C. § 112, first paragraph, also be withdrawn.

7. Claims 13, 14, 22-29, 37, 40, 50 and 51 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. Specifically, the examiner stated that the issue is not whether the particular hybridoma produces CD4-specific antibodies, but rather immunoglobulins that comprise a limited or discrete sequence (*e.g.*, SEQ. ID NO:1) such as the claimed elements set forth in claims 13-14 and claims 22-30 would have the property of binding CD4.

The examiner invited Applicants to consider claiming CD4-specific human monoclonal antibodies with all of the appropriate sequences that provide for binding CD4. Accordingly, Applicants have amended the claims as suggested by the examiner. Therefore, the claims were amended for clarification and to expedite prosecution and not to overcome any rejection based on prior art.

Applicants reemphasize for the record that claims 13, 14, 22-29, 37, 40, 50 and 51 are enabled by the specification as filed, *inter alia*, in Examples 40 and 41, pages 248 to 252 and 252 to 257, respectively. In particular, on page 248, lines 34 to 38, Example 40 notes that cells from 10 individual hybridoma cell lines (1E11, 1G2, 6G5, 10C5, 1G1, 6C1, 2E4, 7G2, 1F8 and 4D1) that secrete human IgG kappa mAbs reactive with human CD4 were derived from JHD/JCKD/HC2/KCo5 transgenic mice. Objective evidence that these human IgG kappa mAbs bind human CD4 with high affinity is provided, *inter alia*, in Tables 17, 18, 19, and 21. On page 253, lines 5 to 37, Example 41 states that cells from five of these hybridoma cell lines (1E11, 1G2, 6G5, 10C5, and 4D1) were used to isolate RNA encoding each of the individual antibodies. *Each of the hybridomas tested produced only one functional heavy and light chain RNA transcript.* The RNA was used as a substrate to synthesize cDNA, which was then used to amplify human Ig gamma and kappa transcript sequences by PCR using primers specific for human VH, Vkappa, Cgamma, and Ckappa. The amplified Ig heavy and kappa light chain sequences were cloned into bacterial plasmids and nucleotide sequences determined. Analysis of the sequences spanning the heavy chain VDJ and light chain VJ junctions revealed in-frame heavy and light chain transcripts for each of the 5 clones. Nucleotide sequences for each of the ten functional transcripts are assigned the SEQUENCE ID NOs: 1E11 gamma (SEQ ID NO:1); 1E11 kappa (SEQ ID NO:2); 1G2 gamma (SEQ ID NO:3); 1G2 kappa (SEQ ID NO:4); 6G5 gamma (SEQ ID NO:5); 6G5 kappa (SEQ ID NO:6); 10C5 gamma (SEQ ID NO:7); 10C5 kappa (SEQ ID NO:8); 4D1 gamma (SEQ ID NO:9); 4D1 kappa (SEQ ID NO:10); see Table 22.

Finally, it is noted (on page 256, lines 16 to 18) that analysis of these DNA sequences demonstrates that the 5 hybridoma clones represent descendants of 4 individual primary B cells. Table 23 (pages 256 to 257) shows the amino acid sequences derived for each of the ten CD4-binding CDR3 regions, and the assignments for germline gene segments incorporated into each of the genes encoding these transcripts. These CDR3 regions include SEQ ID NO:63 in clone 1E11 (*i.e.*, DITMVRGVPH) , SEQ ID NO:64 in clone 1G2 (*i.e.*, PANWNWYFVL), SEQ ID NO:65 in clone 6G5 (*i.e.*, VINWFDP), SEQ ID NO:66 in clone 4D1 (*i.e.*, DQLGLFDY), SEQ ID NO:67 in clone 1E11 (*i.e.*, QQYGSSPLT), SEQ ID NO:68 in clone

1G2 (*i.e.*, QQFISYPQLT), SEQ ID NO:69 in clone 6G5 (*i.e.*, QQANSFPYT), SEQ ID NO:70 in clone 4D1 (*i.e.*, QQYDSYPYT).

Accordingly, the specification as filed sufficiently describes and enables claims claims 13, 14, 22-29, 37, 40, 50 and 51 to satisfy the requirements of section 112, first paragraph, including providing objective evidence that human monoclonal immunoglobulins comprising these sequences can bind human CD4.

8. Claim 35 and 38 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not described in the specification under 37 C.F.R. § 1.801-1.809.

The rejection of claims 35 and 38 is mooted by the cancellation without prejudice of the rejected claims. Therefore the rejection of claims 35 and 38 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not described in the specification under 37 C.F.R. § 1.801-1.809 should be withdrawn

Objection Under 37 C.F.R. 1.75(c)

10. Claim 38 was objected to under 37 C.F.R. § 1.75(c), as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim.

As noted above, claim 38 was canceled without prejudice. Therefore the objection of claim 38 37 C.F.R. § 1.75(c), as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim should be withdrawn.

Rejections Under 35 U.S.C. § 112, second paragraph

11. Claim 13, 14, 35 and 38 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Specifically, the examiner alleged that claims 13 and 14 were indefinite in the recitation of "similar affinity" because the phrase is relative in nature which renders the claim indefinite. The examiner also stated that claims 35 and 38 are indefinite in the recitation of "1E11, 1G2, 6G5, 10C5, 1G1, 6C1, 2E4, 1F8, 4D1" because their characteristics allegedly not known.

Applicants amended claim 13 to expedite prosecution, not to overcome any rejection based on prior art, rendering the rejection under 35 U.S.C. § 112, second paragraph,

moot. Again, as noted above, the rejection of claims 35 and 38 is mooted by the cancellation of these claims without prejudice.

Therefore, the rejection of claims 13, 14 (as well as claims 51 and 53), 35 and 38 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite should be withdrawn.

Rejections Under 35 U.S.C. § 103(a)

16. Claims 10, 12, 18-21, 31-34, 38-39, 41-49 were rejected under 35 U.S.C. § 103(a) as obvious over Cobbold *et al.* (U.S. Patent No. 5,690,933) and Queen *et al.* (U.S. Patent No. 5,530,101).

The rejection of claims 10, 12, 18-21, 31-34, 38-39, 41-49 has been mooted by cancellation of these claims without prejudice. Claims 10, 12, 18-21, 31-34, 38-39, 41-49 were canceled to expedite prosecution and not to overcome any rejection based on prior art.

Therefore the rejections claims 10, 12, 18-21, 31-34, 38-39, 41-49 under 35 U.S.C. § 103(a) under 35 U.S.C. 103(a) as obvious over Cobbold *et al.* (U.S. Patent No. 5,690,933) and Queen *et al.* (U.S. Patent No. 5,530,101) should be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

ext 5324

Respectfully submitted,

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